CLAIMS

We claim:

1. A targeting construct comprising:

(a) a first polynucleotide sequence homologous to an intestinal alkaline phosphatase gene;

(b) a second polynucleotide sequence homologous to the intestinal alkaline phosphatase gene; and

(c) a selectable marker.

2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.

3. A method of producing a targeting construct, the method comprising:

(a) providing a first polynucleotide sequence homologous to an intestinal alkaline phosphatase gene;

(b) providing a second polynucleotide sequence homologous to the intestinal alkaline phosphatase;

(c) providing a selectable marker; and

(d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

4. A method of producing a targeting construct, the method comprising:

(a) providing a polynucleotide comprising a first sequence homologous to a first region of an intestinal alkaline phosphatase gene and a second sequence homologous to a second region of an intestinal alkaline phosphatase gene;

(b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.

5. A cell comprising a disruption in an intestinal alkaline phosphatase gene.

6. The cell of claim 5, wherein the cell is a murine cell.

7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.

8. A non-human transgenic animal comprising a disruption in an intestinal alkaline phosphatase gene.

9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene, the method comprising:

(a) introducing the targeting construct of claim 1 into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of an intestinal alkaline phosphatase, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in an intestinal alkaline phosphatase gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of intestinal alkaline phosphatase in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of an intestinal alkaline phosphatase, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in an intestinal alkaline phosphatase gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted intestinal alkaline phosphatase gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of intestinal alkaline phosphatase, the method comprising:

(a) providing a cell comprising a disruption in an intestinal alkaline phosphatase gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the intestinal alkaline phosphatase is modulated.

14. A method of identifying an agent that modulates the function of an intestinal alkaline phosphatase gene, the method comprising:

(a) providing a cell comprising a disruption in an intestinal alkaline phosphatase gene;

(b) contacting the cell with an agent; and

(c) determining whether the function of the intestinal alkaline phosphatase gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: nociceptive disorder, abnormal sensitivity to temperature, abnormal sensitivity to pain, activity disorder, anxiety disorder.

18. The transgenic mouse of claim 17, wherein the nociceptive disorder is increased pain response relative to a wild-type mouse.

19. The transgenic mouse of claim 17, wherein the abnormal sensitivity to temperature is increased thermal sensitivity relative to a wild-type mouse.

20. The transgenic mouse of claim 17, wherein the abnormal sensitivity to temperature decreased latency to lick hindpaw during a Hot Plate test relative to a wild-type mouse.

21. The transgenic mouse of claim 17, wherein the abnormal sensitivity to pain is increased pain response relative to a wild-type mouse.

22. The transgenic mouse of claim 17, wherein the abnormal sensitivity to pain is increased sensitivity to heat relative to a wild-type mouse.

23. The transgenic mouse of claim 17, wherein the activity disorder is decreased activity relative to a wild-type mouse.

24. The transgenic mouse of claim 17, wherein the wherein the activity disorder is hypoactivity.

25. The transgenic mouse of claim 17, wherein the wherein the activity disorder is decrease in average movement velocity during the Open Field test relative to a wild-type mouse.

26. The transgenic mouse of claim 17, wherein the anxiety is reduced anxiety relative to a wild-type mouse.

27. A method of producing a transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a nociceptive disorder, an abnormal sensitivity to temperature, an abnormal sensitivity to pain, an activity disorder, or an anxiety disorder, the method comprising:

(a) introducing an intestinal alkaline phosphatase gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene.

28. A cell derived from the transgenic mouse of claim 17 or claim 27.

29. A method of identifying an agent that ameliorates a phenotype associated with a disruption in an intestinal alkaline phosphatase gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: a nociceptive disorder, an abnormal sensitivity to temperature, an abnormal sensitivity to pain, an activity disorder, or an anxiety disorder.

30. A method of identifying an agent that modulates intestinal alkaline phosphatase expression, the method comprising:

(a) administering an agent to the transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene; and

(b) determining whether the agent modulates intestinal alkaline phosphatase expression in the transgenic mouse, wherein the agent has an effect on at least one of the following behaviors: latency to lick hindpaw during a hot plate test or hypoactivity.

31. A method of identifying an agent that modulates a behavior associated with a disruption in an intestinal alkaline phosphatase gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in an intestinal alkaline phosphatase gene; and

(b) determining whether the agent modulates activity or nociception.

32. A method of identifying an agent that modulates intestinal alkaline phosphatase gene function, the method comprising:

(a) providing a cell comprising a disruption in an intestinal alkaline phosphatase gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates intestinal alkaline phosphatase gene function, wherein the agent modulates a phenotype associated with a disruption in an intestinal alkaline phosphatase gene.

33. The method of claim 32, wherein the phenotype comprises at least one of the following: a nociceptive disorder, an abnormal sensitivity to temperature, an abnormal sensitivity to pain, an activity disorder, or an anxiety disorder.

34. An agent identified by the method of claim 29, claim 30, claim 31, or claim 32.